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REMARKS

Claims 15 - 32 and 34 - 40 are pending in the application. Claims 1-14 and 33 have been cancelled herein without prejudice. Applicants retain the right to file further continuation and divisional applications on any non-elected claim and on the subject matter of any claim previously or presently canceled.

With this Amendment, Claim 15 has been amended to clarify what Applicants consider the subject matter of the invention. Support for the amendment to Claim 15 is found in the specification as originally filled, including paragraphs [0021] and [0036], for example. No new matter is introduced by these amendments.

Drawings

Applicants herein submit two (2) sheets of formal drawings in black and white with Figures 1-6. These sheets replace the color informal drawings originally filed with the application.

Claim Rejections under 35 USC §112, first paragraph

The Claims Meet the Written Description Requirement

The Patent Office has rejected Claims 15 - 32, and 34 - 40 under 35 USC §112, first paragraph, as allegedly not meeting the written description requirement. In particular, the Patent Office argues that the specification contains subject matter which was not described in the specification in such a way as to reasonable convey to one skilled in the art that the inventors at the time the application was filed, had possession of the claimed invention (Office Action, page 5). Applicants must respectfully disagree.

The Patent Office states that specification is silent with regard to the specific components present in the inducing feed composition end products (Office Action, pages 4 - 5). Moreover, the specification is silent as to what times and temperatures are required to obtain an inducing feed composition with certain components (Office Action,

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pages 4 - 5). The specification defines inducing feed as "a solution fed to a microorganisms that causes or induces the production of desired protein product" (see specification at page 13), and the Patent Office alleges that this is insufficient to meet the written description requirement. Applicants respectfully disagree.

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. See, e.g., *Moba, B.V. v. Diamond Automation, Inc.*, 325 F.3d 1306, 1319, 66 USPQ2d 1429, 1438 (Fed. Cir. 2003); *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d at 1563, 19 USPQ2d at 1116. An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997).

The present invention provides *methods* for improved protein production from a cell culture using culture components and conditions that dramatically increase the amount of protein produced. The improved methods can be used for the production of proteins encoded by naturally occurring cellulase genes as well as from various heterologous constructs.

The claimed invention requires that the *method* use an inducing feed composition as a component of the feed stream (either batch or continuous) to induce cellulase production or proteins under the control of certain promoters. Lactose is the usual carbon source used in the production of cellulases. Sophorose is the most potent inducer of cellulase expression. Glucose, the main component of the inducing feed composition, although less expensive than both lactose and sophorose, represses cellulase expression. The inventors have found that the production costs of proteins regulated by certain promoters can be reduced by using an in situ cellulase-treated concentrated glucose solution described by the present invention.

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The Patent Office states that the claimed method contains only one active step: providing a host cell with an inducing feed composition (Office Action, page 3). For sake of clarity, Applicants have amended independent Claim 15 to include the steps of (a) Mixing (b) Incubating and (c) Culturing.

Applicants respectfully submit that the written description requirement for Claims 15-32, and 34-40 under 35 USC §112, first paragraph, is satisfied. As described below, the patent specification describes the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention.

As cited by the Patent Office, the specification defines inducing feed as "a solution fed to a microorganisms that causes or induces the production of desired protein product" (see specification at page 13) (Office Action, page 4). Furthermore, in paragraph [0057], the specification as filed recites: "Induction" refers to the increased transcription of a gene resulting in the synthesis of a protein of interest in a cell or organism at a markedly increased rate in response to the presence of an "inducer". To measure the induction of a protein of interest, cells treated with a potential inducer are compared to control samples without the inducer. Control samples (untreated with inducers) are assigned a relative protein activity value of 100%. Induction of a polypeptide is achieved when the activity value relative to the control (untreated with inducers) is greater than 100%, greater than 10%, more preferably 150%, more preferably 200-500% (i.e., two to five fold higher relative to the control), or more preferably 1000-3000% higher.

In Paragraph [0034], the specification as filed recites: "The inducing feed composition has between about 2 and 25 g/L sophorose. In addition, the inducing feed composition has between about 35 and 60 g/L gentiobiose. See Also Example 1, the resulting inducing feed composition was found to have 16.1 g/L Sophorose, 47.5 g/L Gentiobiose, and approximately 600 g/L Glucose.

In Paragraph [0036], the specification as filed recites: The solution is incubated at 50°C - 75°C , preferably between 50° C. and 65 ° C. The solution is incubated for

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between 8 hours and 7 days with mixing. In one embodiment the incubation period is greater than two days. In second embodiment the incubation period is two days. In third embodiment the incubation period is three days.

As set forth above the specification describes the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. Therefore, Applicants respectfully request that the rejection of Claims 15-32, and 34-40 under 35 USC §112, first paragraph, as allegedly not meeting the written description requirement be withdrawn and the Claims passed to allowance.

The Claims are Novel

The Patent Office has rejected Claims 15-28, 31-32 and 34-40 under 35 USC §102(b), as allegedly being anticipated by Mitchinson *et al.* (US Pat. No. 6,268,328), herein after "*Mitchinson*". Claims 15-28, 31-32 and 34-40 stand rejected under 35 USC §102(e) as being anticipated by Fowler *et al.* (US Pat. No. 6,407,046), herein after "*Fowler*". In addition, Claims 15-18 and 23-29 stand rejected under 35 USC §102(e) as being anticipated by Lehmbeck (US Pat. No. 6,352,841), herein after "*Lehmbeck*".

Rejections under 35 U.S.C. §102(b)

The Patent Office has rejected Claims 15-28, 31-32 and 34-40 under 35 USC §102(b), as allegedly being anticipated by *Mitchinson*. Applicants respectfully traverse the rejection.

To anticipate a claim a prior art reference must contain each and every element within the four corners of the document. Thus, Applicants submit that there can be no anticipation unless all of the same elements of the invention are found within the four corners of a single reference. *Lewmar Marine, Inc. v. Barient, Inc.*, 827 F.2d 744, 747, 3 USPQ2d 1766, 1767-68 (Fed. Cir. 1987). A reference that merely contains substantially the same elements or only broadly teaches the invention is insufficient to

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establish anticipation. *Jamesbury Corp. v. Litton Industrial Products, Inc.*, 756 F.2d 1556, 1560, 225 USPQ 253, 258 (Fed. Cir. 1985).

The Patent Office asserts that "the "steps" recited with regard to the production of said inducing feed composition are deemed to constitute a "product by process" description of the recited inducing feed composition" (Office Action, page 8). In Product-by process type claims, the process of producing the product is given no patentable weight since it does not impart novelty to a product when the product is taught by the prior art (*Id.*).

Applicants respectfully assert that the Patent Office's reliance on the case law regarding a product-by-process is not applicable to the *method* claims at issue in the present application. Applicants assert that an invention is defined in a product-by-process claim is a *product*, not a process. In *re* Bridgeford, 357 F.2d 679, 149 USPQ 55 (CCPA 1966). Here the present Claims 15 - 32 and 34-40 are directed to *methods* for producing a protein of interest.

In the present Office Action the Patent Office asserts that *Mitchinson* discloses methods of recombinantly producing cellulases utilizing host cells comprising expression vectors wherein said host cells can be either bacterial, yeast, or fungal. *Mitchinson* further disclose that the bacterial host cells can be either *Bacillus subtilis* and the fungal host cells can be *Trichoderma reesei*. Moreover, *Mitchinson* disclose that the expression vector further comprises an inducible promoter and that said promoter can be *cbh1*. Additionally, *Mitchinson* disclose that the expressed protein can be heterologous to the host cells. While *Mitchinson* do not explicitly disclose that the promoters used are sophorose or gentiobiose inducible, the disclosed *cbh1* promoter possesses these characteristics. (Office Action, Page 9).

Applicants assert that *Mitchinson* fails anticipate Claims 15-28, 31-32 and 34-40 under 35 USC §102(b). For example, independent Claim 15 specifically recites the steps of:

a) Mixing a concentrated glucose solution comprising between about 5% to about 75% glucose with a cellulase preparation selected from the group consisting of a

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whole cellulase composition or beta-glucosidase enriched cellulase composition to give a first mixture;

b) Incubating the first mixture at a temperature and for a sufficient time to produce an inducing feed composition; and

c) Culturing a host cell with said inducing feed composition in an amount effective to induce the production of said protein of interest;" and the remaining claims depend from Claim 15.

While *Mitchinson* states that "Any growth medium can be used in the present invention that is suitable to grow the desired transformants" and refers to a "liquid media" it lacks the steps required of independent Claim 15 (a) - (c), and the claims dependent thereon.

Accordingly Applicants respectfully request the rejection of Claims 15-28, 31-32 and 34-40 in light of *Mitchinson* under 35 USC §102(b) withdrawn.

Rejections under 35 U.S.C. §102(e)

Claims 15-28, 31-32 and 34-40 stand rejected under 35 USC §102(e) as being anticipated by *Fowler et al.* (US Pat. No. 6,407,046). In addition, Claims 15-18 and 23-29 stand rejected under 35 USC §102(e) as being anticipated by *Lehmbeck* (US Pat. No. 6,352,841). Specifically, the Patent Office asserts that *Fowler* and *Lehmbeck* each teach all the limitations of the claimed invention. Applicants respectfully traverse the rejections.

As described in the prior Response to Office Action, the disclosure of *Fowler* is virtually identical to the *Mitchinson* disclosure. Accordingly, for the reasons given above related to the *Mitchinson* reference, Applicants assert that the *Fowler* reference fails to anticipate the claimed invention. Accordingly Applicants respectfully request the rejection of Claims 15-28, 31-32 and 34-40 in light of *Fowler* under 35 USC §102(e) withdrawn.

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In the present Office Action the Patent Office states that *Lehmbeck* discloses methods of recombinant producing cellulases utilizing fungal host cells. *Lehmbeck* further discloses that the fungal host cells can be *Trichoderma reesei* or *Penicillium* species (see column 3, lines 23-32). Moreover, *Lehmbeck* discloses that the expression vectors further comprise an inducible promoter and that the expressed protein can be heterologous to the host (see column 3, lines 13-14) (Office Action, page 15).

The *Lehmbeck* reference, neither expressly or inherently, anticipates the limitations set forth in the pending claims. Again, Claim 15 specifically recites the steps of:

- a) Mixing a concentrated glucose solution comprising between about 5% to about 75% glucose with a cellulase preparation selected from the group consisting of a whole cellulase composition or beta-glucosidase enriched cellulase composition to give a first mixture;
- b) Incubating the first mixture at a temperature and for a sufficient time to produce an inducing feed composition; and
- c) Culturing a host cell with said inducing feed composition in an amount effective to induce the production of said protein of interest;" and the remaining claims depend from Claim 15.

Lehmbeck, like *Fowler* and *Mitchinson* lacks the steps required of independent Claim 15 (a) - (c), and the claims dependent thereon. Accordingly, Applicants respectfully request the withdrawal of the rejections of Claims 15-28, 31-32 and 34-40 in light of *Lehmbeck* under 35 USC §102(e).

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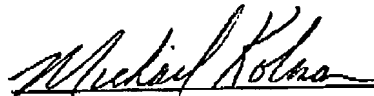
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CONCLUSION

As all of the Examiner's rejections and arguments have been herein addressed and in light of the above remarks, the Applicants respectfully submit that the pending claims are in condition for allowance. Thus, Applicants respectfully request that a Notice of Allowance be issued at an early date. If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (650) 846-7614.

Respectfully submitted,

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